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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,437	03/20/2006	Walter Gumbrecht	32860-000900/US	6672

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EXAMINER	
THOMAS, DAVID C	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
01/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,437	GUMBRECHT ET AL.	
	Examiner	Art Unit	
	David C. Thomas	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *11-15 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 16-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/20/2005; 1/25/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-10 and 16-18 in the reply filed on November 8, 2007 is acknowledged. Claims 11-15 and 19 are withdrawn from further prosecution. The traversal is on the grounds that there is no burden searching both groups. However, this application is filed under 35 U.S.C. 371 and therefore, restriction is based on lack of unity, not search burden. Since the cited X reference (Giles et al. WO 00/58522), as well as other X references, teach electronic detection of the hybridization of amplification products at specified test sites on a microchip, there if no single inventive concept under PCR Rule 13.1.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

2. Claim 16 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 4. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-4, 7, 8, 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Cheng et al. (U.S. Patent Pub. 2002/0155586).

Cheng teaches a method for PCR amplification and detection of nucleotide sequences (for overview, see Abstract), comprising:

using an array of a plurality of microspots forming analytical positions (a flow cell comprises an electronically addressable microarray, paragraph 60, lines 1-6 and Figure 5), said microspots including as probe molecule at least one immobilized oligonucleotide which is hybridizable with a target sequence to be identified of a DNA fragment (nucleic acid probes are attached to the microarray for the purpose of detection of nucleic acids of interest such as amplification products, paragraph 34, lines 1-8 and paragraph 91, lines 1-8);

applying an analyte solution including PCR reagents and a plurality of target sequences to the microspots in such a way that it completely covers the array (the flow cell provides a compartment for containing biological sample materials and buffers to be layered on top of the microchip, including those needed for PCR amplification, paragraph 55, lines 5-15 and paragraph 61, lines 4-6);

subjecting the array to a thermocycling process to amplify the target sequences (heating element, part 12 of Figure 5, can be used for temperature cycling for nucleic acid PCR amplification within the flow cell, paragraph 56, lines 8-12 and paragraph 77, lines 7-11); and

detecting hybridization events on probe molecules immobilized at one analytical position with the aid of a microelectrode arrangement (target species such as amplified

products are electronically addressed to specified capture pads or coated electrodes for capture by anchored capture oligonucleotides, paragraph 92, lines 1-5, for detection using fluorophore-labeled reporter probes and a CCD-based optical imaging system, lines 12-16).

With regard to claims 2-4 and 16, Cheng teaches a method wherein a hydrophilic reaction layer, such as a hyrdogel based on acrylamide and having coupling groups for covalent binding of probe molecules is used (paragraph 60, lines 14-21 and paragraph 92, lines 1-10).

With regard to claims 7, 8 and 17 Cheng teaches a method wherein an analyte solution is used which includes an external primer pair (a concentrated amplification reagent is introduced into the flow cell and contains primer pairs flanking the spa Q and inv A gene target region such that any variations with the genes will be amplified, paragraph 79, lines 6-15 and paragraphs 80-83).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheng et al. (U.S. Patent Pub. 2002/0155586) in view of Ghodsian, B. (U.S. Patent Pub. No. 2002/0115293).

Cheng teaches the limitations of claims 1-4, 7, 8, 16 and 17, as discussed above.

With regard to claim 5, Cheng also teaches a method wherein a biochip including a substrate layer and an insulating layer connected therewith is used, the side of the insulating layer, which faces away from the substrate layer, carrying the electrode arrangement and the reaction layer (an electronically addressable microarray is mounted onto a substrate, to the back of which is attached a ceramic heater, while a protective permeation layer coats the microchips, facing away from the substrate, and protects the biomaterials from being directly exposed to the electrodes in the microchips, paragraph 60, lines 1-21 and Figure 5).

Cheng does not teach a method using a biochip comprising a substrate comprising a semiconductor layer wherein the layer is a silicon layer.

Ghodsian teaches the making of and use of devices for DNA sequencing including lab-on-a-chip devices comprising a substrate that are semiconductors

composed of silicon that are useful for integration of active circuits (paragraph 201, lines 1-11).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the methods of Cheng for making and using an integrated system such as a chip for amplification and detection of nucleic acid targets directly on the chip device with the methods of Ghodsian for making and using similar lab-on-a-chip devices for DNA sequencing since both systems use devices comprising substrates with integrated electronic circuitry for performing or controlling biological reactions, including DNA synthetic processes such as PCR and DNA sequencing. Thus, an ordinary practitioner would have been motivated to combine the methods of Cheng and Ghodsian since the substrates taught by Cheng are highly suitable for being formed of the semiconductor silicon as taught by Ghodsian since this material is ideal for micromachining and the integration of electronic circuits (Ghodsian, paragraph 201, lines 1-7) needed for detection of hybridization of amplified products to capture probes immobilized in a reaction layer, which can be attached to the silicon substrate in the device of Cheng to form the bottom layer of the flow chamber (Cheng, paragraph 61, lines 1-6).

8. Claims 9, 10 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheng et al. (U.S. Patent Pub. 2002/0155586) in view of Strizhkov et al. (BioTechniques (2000) 29:844-846, 848, 850-852, 854, 856-857).

Cheng teaches the limitations of claims 1-4, 7, 8, 16 and 17, as discussed above.

Cheng does not teach a method wherein a target that is first amplified in solution using an external primer and wherein the products are further amplified using internal primers immobilized within a reaction layer.

With regard to claim 10, Fuchs teaches a method wherein an analyte solution is used in which an internal primer pair specifically hybridizing with a target sequence is immobilized in a microspot.

Strizhkov teaches a method of PCR amplification on a microarray using solution-based forward and reverse primers as well as internal primers immobilized inside a gel pad (p. 848, column 1, line 46 to column 2, line 17).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the methods of Cheng for making and using an integrated system such as a chip for amplification and detection of nucleic acid targets directly on the hyrdogel layer of the chip device with the methods of Strizhkov, who also teaches methods of PCR amplification on a microarray using primers both in solution and immobilized on a surface such as a gel pad. Thus, an ordinary practitioner would have been motivated to combine the methods of Cheng and Strizhkov since the methods of PCR amplification taught by Strizhkov using both solution-phase outer primers and solid-phase inner primers can be readily adapted to the microarray methods of Cheng wherein amplification can first take place, as it normally does, in the chamber of the flow cell using solution-based outer primers, followed by capture of the amplification products by immobilized capture probes that also serve as inner forward primers to initiate a second round of amplification on the surface of the hydrogel layer.

This modified system is similar to nested primer amplification and is useful for increasing the specificity of the procedure (Strizhkov, p. 848, column 2, lines 12-16). Amplification products can then be detected with the microelectrode system of Cheng using either light-based detection or a direct electrochemical detection system (Cheng, paragraph 95, lines 7-11).

Conclusion

9. Claims 1-10 and 16-18 are rejected. No claims are allowable.

Correspondence

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David C. Thomas whose telephone number is 571-272-3320 and whose fax number is 571-273-3320. The examiner can normally be reached on 5 days, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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